Interrelationship of architecture and function of the right ventricle

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Armour, J. A., J. B. Pace, and W. C. Randall. Interrelationship of architecture and function of the right ventricle. Am. J. Physiol. 218(1): 174-179, 1970.—The sequence of contraction and augmentation patterns in contractile force of the sinus and conus regions of the right ventricle were analyzed under control, vagal, and sympathetic stimulation as well as norepinephrine infusion states. The normal peristaltic contraction wave from sinus to conus was exaggerated during vagal stimulation but made more nearly synchronous or even abolished during stellate ganglion stimulation. The sinus to conus sequence was often reversed as a result of norepinephrine augmentation. Whereas the conus fibers showed greater increase in force of contraction than did the sinus fibers during stellate stimulation and norepinephrine injection, pressures recorded from the sinus portion of the right ventricle greatly exceeded those measured simultaneously from the conus. A marked intraventricular pressure gradient was created from sinus to conus, with a relatively smaller gradient from conus to pulmonary artery. Thus, the functional interdependence of the infundibular region of the right ventricle as a pressure regulator protecting the pulmonary vasculature may be hypothesized.

Materials and Methods

Sixteen open-chest dogs, weighing 15-20 kg, were studied under phencyclidine hydrochloride (2 mg/kg iv) and α-chloralose (60-80 mg/kg iv) anesthesia and positive-pressure respiration. Four modified Walton-Brodie strain-gauge arches, with essentially linear recording characteristics up to 100 g weight deflection, were sutured to the anterior epicardial surfaces of the right ventricle. The limbs of the gauges were compressed so that the underlying myocardium was stretched significantly. The axis of gauge placement coincided with the major direction of the underlying myocardial fibers. The gauges were positioned as follows: 1) the conus, the major axis being circumcircular, with the sutures located 4 to 5 mm proximal to the pulmonic valve ring; 2) the midposition, just below the left border of the tricuspid valve; 3) the anterior border of the right ventricle (the main sinus region) at an approximately 30° from the vertical (base to apex); 4) the lateral border of the right ventricle (the main sinus region) at approximately 20° from the vertical, parallel to the superficial fibers; 4) sometimes a fourth gauge was placed parallel to and between the second and third gauges. The sutures were superficially placed so that the underlying tissue was held taut and the direction of fibers under the gauge was uniform. In five experiments the gauges were switched from one position to another in order to insure that the contractile force changes were not gauge dependent, but represented a true function of the underlying myocardium. Walton-Brodie gauges are considered to record essentially isometric force from underlying myocardial segments (8). The maximal force and rate of development of force were measured during different interventions and compared as percent change from control values; maximal rate of force development was measured as the steepest slope of the contraction curve. The gauge outputs were recorded on either a Grass polygraph or a four-channel Tektronix cathode-ray oscilloscope.

The right ventricle develops embryologically from two separate components to function in an integrated manner as the sinus (inflow) and conus (outflow) regions. Retention of the circumvascular muscles of the primitive bulbus cordis differentiates the right chamber into these two functional regions (10). Analysis of the functional characteristics of the right ventricular outflow tract has been stimulated by investigations concerned with elucidation of infundibular stenosis in man (3). However, little functional significance has been given to right ventricular contraction patterns (1, 9, 21). Recent considerations of the functional characteristics of the inflow and outflow regions showed that right ventricular systole is characterized by a sequential contraction beginning at the inflow tract and extending into the conal region (4, 14, 16). In addition, these two anatomically divisible regions can develop markedly different intracavity pressures during inotropic interventions (15). The present study was designed to gain insight into the relations between the simultaneous development of contractile force and the generation of intracavitary pressures within the sinus and conus regions.
RIGHT VENTRICULAR STRUCTURE AND FUNCTION

FIG. 2. Tracing from an oscilloscope demonstrates forces recorded from Walton-Brodie gauges on same three regions as in Fig. 1. First trace is from bulk of sinus musculature, followed by force gauge on the sinus adjacent to conus region. Tracing on right is recorded from conus. Onset of sinus contraction preceded that in conus by 50 msec. Vertical lines are 50 msec apart.

(model S5) at parameters of 2–5 v, 4 msec, and 4 cycles/sec, before and after atropine. Augmented contraction of the right ventricle was also elicited by the intravenous administration of 1.0 µg/kg of norepinephrine diluted in 2 ml of normal saline.

RESULTS

Figure 1 illustrates the simultaneous responses in contractile force from the three regions of the right ventricle. Fast traces during control and stimulation (right stellate) periods permit comparison of the rate of development in contractile force (dF/dt) as well as the maximal force. The contractile force of the conus increased 100%, whereas that of the paracanal (mid) and sinus regions increased 70 and 60%, respectively; dF/dt increased 177% on the conus segment and 138% on the sinus segment. It is of interest that mechanical alternans appeared during the period of stimulation on the midventricular segment but was absent from each of the other regions of the right ventricle. The onset of sinus contraction preceded that in conus by 6–12 msec.

Oscilloscopic traces from gauges recording contractile force from identical positions of the right ventricle from another animal illustrates the precedence of sinus contraction (Fig. 2). The earliest onset of contraction occurred in the main sinus region, followed in 20 msec by the paracanal segment with conal contraction 30 msec later. Time intervals required for attainment of maximum force followed a similar sequence. Thus, a major fraction of sinus musculature was recruited considerably in advance of that of the conus.

Figure 3 illustrates changes in both contractile force and in intraventricular pressures accompanying electrical excitation of the left stellate ganglion. In confirmation of earlier reports, augmentation in both contractile force and pressure was more prominent than during right stellate stimulation. The percent increase in contractile force on the conus region markedly exceeded that on the midventricular and lateral (sinus) portions of the right ventricle. Simultaneous measurement of intraventricular pressures, on the other hand, revealed much greater development of intrasinusal pressure as compared with that in the intraconal portion of the ventricle. In the control period the sinus and conus region developed similar pressures; during stellate stimulation the differential pressure developed between the sinus and conus is dramatically illustrated. The minimal pressure increase in the conus is faithfully represented in the pulmonary artery pressure.

Figure 4 reveals simultaneous changes in contractile force as well as in dF/dt on all three portions of the right ventricle during electrical excitation of the right cervical vagosympathetic trunks in the atropinized preparation. Again, augmentation was more prominent in the conus segment. Differences in magnitude of change in contractile force as induced by excitation of right and left vagosympathetics were not significant.

In the absence of atropine, vagal stimulation significantly elongated the interval of time between excitation (as indicated by the Q wave of the ECG) of the ventricle and mechanical contraction of each of the three test regions (P value < 0.001). In addition, the time interval between initial contraction of the sinus and conus musculature was distinctly exaggerated. Alterations in contraction sequence are illustrated in Fig. 5. In order to achieve minimal alterations in contractile force and heart rate, relatively low stimulation intensities (2 v, 4 cycles/sec, 2 msec) were employed. In Fig. 5, heart rate was decreased from 198 to 170 beats/min with little or no change in contractile force or dF/dt. The initial deflection in the conus gauge record was downward during stimulation, suggesting a preliminary distension of the conus segment.

Figure 6 illustrates the simultaneous changes in force and dF/dt resulting from intravenous injection of norepinephrine.
Again, the most prominent increase in force and dF/dt was observed on the conus region, superimposed upon a slight but consistent elevation in base line. Under these experimental conditions, the onset of contraction occurred almost simultaneously in the three regions of the ventricle. Figure 7 is a cathode-ray oscilloscope trace from similar experiment in which the sinus region (solid line) contracted before the conus (broken line) during the control period (upper trace). During the positive inotropic response to norepinephrine (lower trace), the onset of contraction in the conus preceded that in the sinus region by approximately 50 msec. This directional shift in contractile sequence was observed in all animals in which this procedure was carried out.

Table 1 summarizes the comparative responses of the three regions of the right ventricle to electrical stimulation of the right and left vagosympathetic trunks in the atropinized animal. In all experiments, regional responses to stimulation represented statistically significant changes from control force and dF/dt. Comparisons between response of the conus and sinus to vagosympathetic stimulation reveal equally significant changes, the conus showing markedly

![Image of cathode-ray oscilloscope trace](http://ajplegacy.physiology.org/)

FIG. 3. Upper three traces are from strain gauges placed on right ventricle, as in Fig. 1. Lower three traces show sinus and conus intraventricular pressures with the pulmonary artery pressure (PAP). Note that force of contraction from all areas of right ventricle were augmented during left stellate stimulation, with conus force showing greatest augmentation. In contrast, peak intracardiac pressure was minimally elevated. Peak intr sinus pressure was markedly increased.

**FIG. 4.** Effects of right vagosympathetic trunk stimulation after atropine. Force gauges were placed as in previous figures and maximal augmentation occurred in conal region.

**FIG. 5.** Minimal right vagal stimulation elicited a slight bradycardia. Contractile force from various regions was not depressed, but sequence of contraction from sinus to conus was delayed. Conus force gauge recorded a downward deflection when sinus fibers are first contracting.
Infusion of norepinephrine increased force of contraction in all three regions of right ventricle. Conal fibers are augmented almost twice that of rest of right ventricle. Diastolic force base line is elevated in conus and depressed in sinus regions.

FIG. 6. Oscilloscopic tracings of a control period (upper trace) of sinus (solid line) and conus (broken line) force patterns. Lower trace illustrates change in contraction sequence between sinus and conus after infusion of norepinephrine. Onset of conus contraction preceded sinus contraction by 50 msec.

Table 2 summarizes the sequential order of contraction on the same three anatomical zones of the right ventricle during control, vagosympathetic (in absence of atropine), stellate stimulation, and norepinephrine injection. Measuring from the initial deflection in Q wave of the ECG to the beginning of mechanical contraction, the time intervals are compared. Control measurements were performed early in the experiment, at which time the sequence of contraction was regularly from sinus to conus. Following repeated sympathetic stimulation, or as the preparation progressively deteriorated, these intervals were shortened and contraction frequently became more nearly synchronous.

Vagal bradycardia induced by stimulating voltages sufficient to maintain sinus rhythm, invariably prolonged the time interval in each of the test regions. The interval from onset of Q wave to contraction of the conus was most strikingly extended.

Both right stellate stimulation and norepinephrine injection induced an opposite change in which the interval was markedly shortened until the three regions contracted more nearly simultaneously. Indeed, norepinephrine consistently reversed the sequence so that conus contraction preceded that of the sinus. All of these alterations were found to be statistically significant ($P = .001$).

**DISCUSSION**

The right ventricle is considered a low-pressure volume pump (20) and its function has been minimized to the point of questioning whether it is required to move blood (9). Strain gauges are frequently applied to the conus to record changes in contraction thought to be characteristic of the right ventricle and often treated as typical of the entire heart. Interest in its function may be focused upon certain
peak force and maximum $dF/dt$ in cunus, Faraconal sinus, and sinus force is invariably higher on the cunus region, intracavity sinus, and cunus tabulated as interval between Q wave and onset of force from various regions.

Inasmuch as the radius of curvature of the cunus is a fifth or sixth that of the sinus chamber (5, 6), fibers creating a physical advantage over the sinus region.

In contrast, the cunus is made up of parallel circumconal fibers. It is apparent that sympathetic fibers carried in the vagosympathetic trunk have similar augmentor actions, with predominant influences also on the conus normally dilates with blood expelled from the sinus. March et al. (14) noted that the conus normally dilates with blood expelled from the sinus.

The effect of sympathetic stimulation is opposite to that of the vagus in relation to pressure generation and sequence of contraction. The acceleration in heart rate and augmentation in rate and force of contraction was expected, but the sequence of contraction was opposite from that observed during vagal stimulation. Thus, sympathetic innervation elicits regional functional alterations in the right heart comparable to those reported for the left heart (17). Sympathetic fibers in the vagosympathetic trunk have similar augmentor actions, with predominant influences also on the conal fibers. It is apparent that sympathetic fibers carried in the vagosympathetic trunk primarily serve the conus region, whereas those from the stellate ganglia provide important innervation to both regions.

When the right ventricle contracts vigorously under stellate stimulation or noradrenaline influence, a visible groove becomes apparent in the region of muscular fiber transition between the sinus and conus. This investigation demonstrated that the conus acts as a resistive element, while the sinus serves as a flow generator (15). Thus, whereas percent increase in contractile force is invariably higher on the conus region, intracavity pressure of the sinus is much higher during positive inotropism (Fig. 3). The fiber architecture of the sinus (inflow tract) is similar to that of the left ventricle (11, 13, 23, 24). In contrast, the conus is made up of parallel circumconal fibers creating a physical advantage over the sinus region inasmuch as the radius of curvature of the conus is a fifth or sixth that of the sinus chamber (5, 6).

Not all reports have been in accord concerning the contractile sequence across the right heart (1, 21). However, a perisystolic wave has been shown to originate from the sinus and pass to the conus (4, 16), with conus contraction occurring approximately 20 msec after the sinus (14). In the present experiments the average interval between sinal and conal contraction was 25 msec, with variations up to 50 msec (Fig. 2). About two-thirds of the delay occurred in the junctional region between the sinus and conus, paraconal sinus contraction following 15 msec after the right lateral border.

Weak vagal stimulation causing bradycardia prolonged the normal sequence of contraction. The sequence of contraction is frequently so delayed that the conus gauge recorded a downward deflection before the usual upward deflection, indicating a separation of the gauge legs by distension of the conus. March et al. (14) noted that the conus normally dilates with blood expelled from the sinus.

Keith (10) observed embryogenic differentiation of the right ventricle into the sinus and conus and proposed that the circumconal fibers act as a safety mechanism, protecting the pulmonic vasculature from high pressures generated in the bulk of the right ventricle. In turtles the circumarterial muscle fibers of the right ventricle can act as a functional stricture directing flow into the systemic circulation (22, 25).

### Table 1: Influence of nerve stimulations and injection of norepinephrine* on heart rate, and percent change from control in peak force and maximum $dF/dt$ in conus, paraconal sinus, and sinus

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Animals</th>
<th>Heart Rate, beats/min</th>
<th>Maximum Force</th>
<th>Maximum $dF/dt$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Conus</td>
<td>Paraconal sinus</td>
<td>Sinus</td>
</tr>
<tr>
<td>Control</td>
<td>16</td>
<td>138 ± 7</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Atropinized right vagus</td>
<td>11</td>
<td>144 ± 13</td>
<td>180 ± 22</td>
<td>126 ± 33</td>
</tr>
<tr>
<td>Atropinized left vagus</td>
<td>11</td>
<td>131 ± 9</td>
<td>159 ± 20</td>
<td>126 ± 5</td>
</tr>
<tr>
<td>Right stellate</td>
<td>12</td>
<td>169 ± 5</td>
<td>213 ± 26</td>
<td>189 ± 22</td>
</tr>
<tr>
<td>Left stellate</td>
<td>12</td>
<td>150 ± 7</td>
<td>253 ± 44</td>
<td>178 ± 21</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>14</td>
<td>193 ± 33</td>
<td>306 ± 84</td>
<td>302 ± 86</td>
</tr>
</tbody>
</table>

Values are means ± SEM. * 1µg/kg.

### Table 2: Time sequence of onsets of contraction as recorded with Walton-Brodie strain gauges on sinus, paraconal sinus, and conus tabulated as interval between Q wave and onset of force from various regions

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Animals</th>
<th>Heart Rate, beats/min</th>
<th>Sinus</th>
<th>Paraconal sinus</th>
<th>Conus</th>
<th>P Value, Conus vs. Sinus</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>16</td>
<td>138 ± 7</td>
<td>52 ± 2</td>
<td>67 ± 3</td>
<td>77 ± 3</td>
<td>&lt;0.001</td>
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<tr>
<td>Vagal bradycardia</td>
<td>11</td>
<td>131 ± 9</td>
<td>77 ± 20</td>
<td>88 ± 14</td>
<td>120 ± 0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right stellate</td>
<td>12</td>
<td>169 ± 5</td>
<td>44 ± 3</td>
<td>48 ± 5</td>
<td>49 ± 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>14</td>
<td>193 ± 33</td>
<td>43 ± 3</td>
<td>36 ± 2</td>
<td>31 ± 3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
in these two regions. Figure 3 demonstrates the greater augmentation of contractile force in the conal fibers compared to the sinus fibers. Thus, the conal fibers appear to create a functional resistive element preventing the high sinus pressure from reaching the pulmonary artery. Norepinephrine causes the conus to contract as much as 40 msec before the sinus regions. This early onset of contraction and the mechanical advantages of the circumferential fibers (5, 6, 22) thus attenuate the effect of the pressure drop from the sinus to the pulmonary vascular tree by means of a functional stricture or pressure regulator (15, 22, 25).

In the conus region the diastolic force base line shifts upward considerably under norepinephrine augmentation (lower trace, Fig. 6) whereas the sinus diastolic base line drops (upper trace, Fig. 6). Presumably this corresponds to the functional stricture or pressure regulator (15, 22, 25). Extra-sinus pressure from reaching the pulmonary artery.

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REFERENCES